Complete Summary

GUIDELINE TITLE

Guidance on the use of glitazones for the treatment of type 2 diabetes.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). Guidance on the use of glitazones for the treatment of type 2 diabetes. London (UK): National Institute for Clinical Excellence (NICE); 2003 Aug. 22 p. (Technology appraisal; no. 63).

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

On January 5, 2006, GlaxoSmithKline and the U.S. Food and Drug Administration (FDA) notified healthcare professionals about post-marketing reports of new onset and worsening diabetic macular edema for patients receiving rosiglitazone. In the majority of these cases, the patients also reported concurrent peripheral edema. In some cases, the macular edema resolved or improved following discontinuation of therapy and in one case, macular edema resolved after dose reduction. See the FDA Web site for more information regarding rosiglitazone.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Type 2 diabetes

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Endocrinology
Family Practice
Internal Medicine

INTENDED USERS

Advanced Practice Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To assess the clinical and cost-effectiveness of glitazones for the treatment of type 2 diabetes

TARGET POPULATION

People with type 2 diabetes

INTERVENTIONS AND PRACTICES CONSIDERED

Glitazones (rosiglitazone, pioglitazone) as second-line therapy added to either metformin or a sulphonylurea

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
  - Haemoglobin A_{1c} [HbA_{1c}] level
  - Cardiovascular risk factors
  - Quality of life
  - Mortality rate
- Cost effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the School of Health and Related Research (ScHARR), University of Sheffield. (See the "Companion Documents" field.)

Search Strategy

Sources Searched

Twelve electronic bibliographic databases were searched, covering biomedical, health-related, science, social science, and grey literature. A list of databases is provided in Appendix 1 of the Assessment Report (see "Availability of Companion Documents" field).

In addition, the reference lists of relevant articles were checked and 14 health services research related resources were consulted via the Internet. These included health technology assessment (HTA) organisations, guideline producing bodies, generic research and trials registers, and specialist diabetes sites. A list of these additional sources is given in Appendix 2 of the Assessment Report (see "Availability of Companion Documents" field). Finally, citation searches of key papers were undertaken using the Science Citation Index (SCI) citation facility and the reference lists of included studies were checked for additional studies.

Search Terms

A combination of free-text and thesaurus terms were used. 'Intervention' terms included: glitazone(s), thiazole(s), thiazolidinedione, peroxisome proliferator-activated receptor (PPAR) gamma agonist(s), pioglitazone, actos, 111025-46-8 (CAS registry number), ad 4833 and u 72107 (product codes), rosiglitazone, avandia, 122320-73-4 (CAS registry number), BRL 49653 (product code). Copies of the search strategies used in the major databases are included in Appendix 3 of the Assessment Report (see "Availability of Companion Documents" field).

Search Restrictions

No date, language, study or publication type restrictions were applied.

NUMBER OF SOURCE DOCUMENTS

Nine studies met the inclusion criteria

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

There were no published economic evaluations investigating the cost effectiveness of the glitazones. The only available cost-effectiveness evidence was that obtained as part of the confidential submissions from the manufacturers.

Both manufacturers submitted economic models. The Assessment Group did not develop its own model, but provided a comprehensive critique of the submitted models.

See Section 4.2 of the original guideline document for a detailed discussion of the cost-effectiveness analysis.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document

(ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

- For people with type 2 diabetes, the use of a glitazone as second-line therapy added to either metformin or a sulphonylurea--as an alternative to treatment with a combination of metformin and a sulphonylurea--is not recommended except for those who are unable to take metformin and a sulphonylurea in combination because of intolerance or a contraindication to one of the drugs. In this instance, the glitazone should replace in the combination the drug that is poorly tolerated or contraindicated.
- The effectiveness of glitazone combination therapy should be monitored against treatment targets for glycaemic control (usually in terms of haemoglobin A_{1c} [HbA_{1c}] level) and for other cardiovascular risk factors, including lipid profile. The target HbA_{1c} level should be set between 6.5% and 7.5%, depending on other risk factors.
- The present United Kingdome licence does not allow the Institute to recommend the use of glitazones in triple combination therapy (with other oral antidiabetic agents), as monotherapy, or in combination with insulin. The use of a glitazone in triple combination (with other oral antidiabetic agents) is classified in the licence under "special warnings and special precautions for use." This precaution is based on the fact that at the time the licence was issued there was no clinical experience of triple combination therapy. When this guidance is reviewed the recommendations will take into account any extensions to the licence for the use of glitazones.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of glitazones for the treatment of type 2 diabetes

POTENTIAL HARMS

- The use of a glitazone in triple combination with other oral antidiabetic agents is classified in the licence under "special warnings and special precautions for use." The Summary of Product Characteristics indicates that this precaution is based on the fact that, at the time the licence was issued, there was no clinical experience of triple combination therapy.
- Because of the association of another thiazolidinedione (troglitazone, now withdrawn) with liver failure, it is currently recommended by both manufacturers of glitazones that patients should have liver function tests before initiation of treatment, then every 2 months for the first year of treatment, and periodically thereafter.

For full details of side effects, precautions, and contraindications, see the Summary of Product Characteristics, available at http://emc.medicines.org.uk/.

CONTRAINDICATIONS

CONTRAINDICATIONS

Neither pioglitazone nor rosiglitazone is licensed for monotherapy or for use in patients who have previously been treated only with diet and exercise. The Summaries of Product Characteristics for both drugs state that they are contraindicated for use in combination with insulin.

For full details of side effects, precautions, and contraindications, see the Summary of Product Characteristics, available at http://emc.medicines.org.uk/.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation and Audit

- National Health Service (NHS) organisations and all clinicians who provide care for people with diabetes, including general practitioners and consultants

treating people with diabetes, should review local practice and policies regarding the use of glitazones for the treatment of people with type 2 diabetes to take account of the guidance (see the "Major Recommendations" field).
- Local guidelines or care pathways that refer to the care of people with diabetes should incorporate the guidance.
- To measure compliance locally with the guidance, the following criteria could be used. Further details on suggestions for audit are presented in Appendix C of the original guideline document.
    - An individual with type 2 diabetes is normally not offered a glitazone as second-line therapy added to either metformin or a sulphonylurea as an alternative to treatment with a combination of metformin and sulphonylurea. The exception is an individual with type 2 diabetes who is unable to take metformin and a sulphonylurea in combination because of intolerance or a contraindication to one of the drugs, in which case the glitazone can be prescribed to replace in the combination the drug that is poorly tolerated or contraindicated.
    - The effectiveness of glitazone combination therapy is monitored against treatment targets for glycaemic control and for other cardiovascular risk factors.
    - Local clinical audits on the care of people with diabetes could also include criteria for the management of diabetes based on the standards in the National Service Framework for Diabetes.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Foreign Language Translations
Patient Resources
Quick Reference Guides/Physician Guides

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). Guidance on the use of glitazones for the treatment of type 2 diabetes. London (UK): National Institute for Clinical Excellence (NICE); 2003 Aug. 22 p. (Technology appraisal; no. 63).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Aug

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Dr Jane Adam, Radiologist, St George's Hospital, London; Dr Sunil Angris, General Practitioner, Waterhouses Medical Practice, Staffordshire; Dr Darren Ashcroft, Senior Clinical Lecturer, School of Pharmacy & Pharmaceutical Sciences, University of Manchester; Professor David Barnett (Chair) Professor of Clinical Pharmacology, University of Leicester; Professor John Brazier, Health Economist, University of Sheffield; Professor Mike Campbell, Statistician, Institute of General Practice & Primary Care, Sheffield; Dr Mike Davies, Consultant Physician, University Department of Medicine & Metabolism, Manchester Royal Infirmary; Dr Cam Donaldson, PPP Foundation Professor of Health Economics, School of Population and Health Sciences & Business School, Business School - Economics, University of Newcastle upon Tyne; Professor Jack Dowie, Health Economist, London School of Hygiene & Tropical Medicine; Dr Paul Ewings, Statistician, Taunton & Somerset NHS Trust, Taunton; Professor Trisha Greenhalgh, Professor of Primary Health Care, University College London; Miss Linda Hands, Clinical Reader in Surgery, University of Oxford; Ms Ruth Lesirge, Lay Representative, previously Director, Mental Health Foundation, London; Dr George Levvy, Lay Representative, Chief Executive, Motor Neurone Disease Association, Northampton; Dr Gill Morgan, Chief Executive, NHS Confederation, London; Professor Miranda Mugford (up to November 2002) Health Economist, University of East Anglia, Norwich; Professor Philip Routledge, Professor of Clinical Pharmacology, College of Medicine, University of Wales, Cardiff; Dr Stephen Saltissi, Consultant Cardiologist, Royal Liverpool University Hospital; Professor Andrew Stevens (Vice-Chair) Professor of Public Health, University of Birmingham;

Professor Mary Watkins, Professor of Nursing, University of Plymouth; Dr Norman Waugh, Senior Lecturer and Public Health Consultant, University of Southampton

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Glitazones for the treatment of type 2 diabetes. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2003 Aug. 1 p. (Technology appraisal 63). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- The clinical and cost-effectiveness of pioglitazone and rosiglitazone in the treatment of type 2 diabetes. Assessment report. NHS R&D HTA Programme; 140 p. Available in Portable Document Format (PDF) from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N0210. 11 Strand, London, WC2N 5HR.

Additionally, Audit Criteria can be found in Appendix C of the original guideline document.

PATIENT RESOURCES

The following is available:

- Glitazones for the treatment of type 2 diabetes. Understanding NICE guidance - information for people with diabetes, and the public. London (UK): National Institute for Health and Clinical Excellence (NICE); 2003 Aug. 9 p. (Technology appraisal 63).

Electronic copies: Available in English and Welsh in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the Department of Health Publications Order Line 0870 1555 455. ref: N0211. 11 Strand, London, WC2N 5HR.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI on June 20, 2006.

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